L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:105938 CAPLUS
DN 128:167354
TI Preparation of substituted pyridines and biphenyls as anti-hypercholesteremic, anti-hyperlipoproteinemic and anti-hyperglycemic agents
IN Schmidt, Gunter; Angerbauer, Rolf; Brandes, Arndt; Muller-Gliemann, Matthias; Bischoff, Hilmar; Schmidt, Delf; Wohlfeil, Stefan; Schoen, William R.; Ladouceur, Gaetan H.; Cook, James H., II; Lease, Timothy G.; Wolanin, Donald J.; Kramss, Richard H.; Hertzog, Donald L.; Osterhout, Martin H.
PA Bayer Corporation, USA; Bayer Aktiengesellschaft
SO PCT Int. Appl., 431 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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OS MARPAT 128:167354
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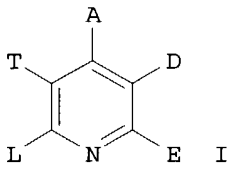

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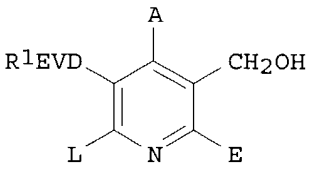

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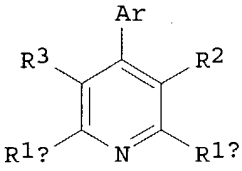

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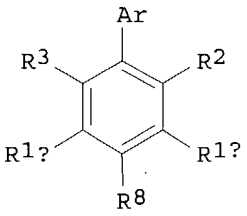


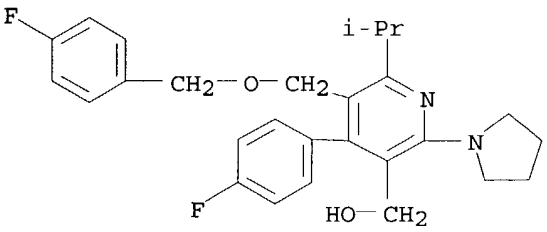
IV

AB The title compds. [I (A = (un)substituted C6-10 aryl; D = up to 8 carbon atoms alkyl which is substituted by hydroxy; E, L = (un)substituted up to 8 carbon atoms alkyl; L = (un)substituted C6-10 aryl; T = R7X, R8C(R9)(R10); R7, R8 = cycloalkyl, aryl, etc.; R9, R10 = H, halo, N3, etc.), II (R1 = cycloalkyl, aryl, etc.; E, D = alkyl (up to 8 carbon atoms); E = a bond; V = O, S, NH, etc.), III (R1a, R1b = CF3, C1-10 alkyl, C1-10 alkenyl, etc.; R2 = C1-10 alkyl, C1-10 alkenyl, etc.; R3 = OH, CF3, C1-6 alkanoyl, etc.; Ar = (un)substituted heteroaryl, aryl), IV], useful for the inhibition of cholesterol ester transfer proteins (CETP) (I), for the treatment of hyperlipoproteinemia (II), and for inhibition of the glucagon receptor, leading to treatment of glucagon-mediated conditions such as diabetes (III-IV), were prepared Thus, reduction of Et 2,6-diisopropyl-4-(4-fluorophenyl)-3-[(4-fluorophenyl)-chloromethyl]pyridine-5-carboxylate (preparation described) with LiAlH4 in THF afforded 69% I [A = 4-FC6H4; D = CH2OH; E = L = iPr; T = 4-FC6H4CH2]. For example, compound I [A = 4-FC6H4; D = CH2OH; E = L = iPr; T = 4-FC6H4CH(NH2)] showed IC50 of 0.6 μM against CETP.

IT **202852-05-9P 202852-97-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted pyridines and biphenyls as anti-hypercholesteremic, anti-hyperlipoproteinemic and anti-hyperglycemic agents)

RN 202852-05-9 CAPLUS

CN 3-Pyridinemethanol, 4-(4-fluorophenyl)-5-[[(4-fluorophenyl)methoxy]methyl]-6-(1-methylethyl)-2-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 202852-97-9 CAPLUS
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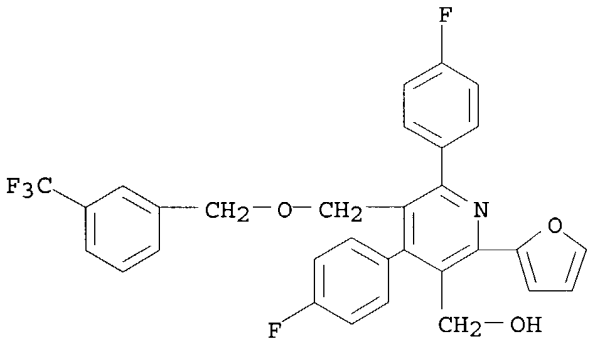

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NEWS 4	DEC 08	INPADOC: Legal Status data reloaded
NEWS 5	SEP 29	DISSABS now available on STN
NEWS 6	OCT 10	PCTFULL: Two new display fields added
NEWS 7	OCT 21	BIOSIS file reloaded and enhanced
NEWS 8	OCT 28	BIOSIS file segment of TOXCENTER reloaded and enhanced
NEWS 9	NOV 24	MSDS-CCOHS file reloaded
NEWS 10	DEC 08	CABA reloaded with left truncation
NEWS 11	DEC 08	IMS file names changed
NEWS 12	DEC 09	Experimental property data collected by CAS now available in REGISTRY
NEWS 13	DEC 09	STN Entry Date available for display in REGISTRY and CA/CAplus
NEWS 14	DEC 17	DGENE: Two new display fields added
NEWS 15	DEC 18	BIOTECHNO no longer updated
NEWS 16	DEC 19	CROPU no longer updated; subscriber discount no longer available
NEWS 17	DEC 22	Additional INPI reactions and pre-1907 documents added to CAS databases
NEWS 18	DEC 22	IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
NEWS 19	DEC 22	ABI-INFORM now available on STN
NEWS 20	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 21	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus

NEWS EXPRESS	DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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NEWS WWW	CAS World Wide Web Site (general information)

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=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
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STRUCTURE FILE UPDATES: 3 FEB 2004 HIGHEST RN 646026-80-4
DICTIONARY FILE UPDATES: 3 FEB 2004 HIGHEST RN 646026-80-4

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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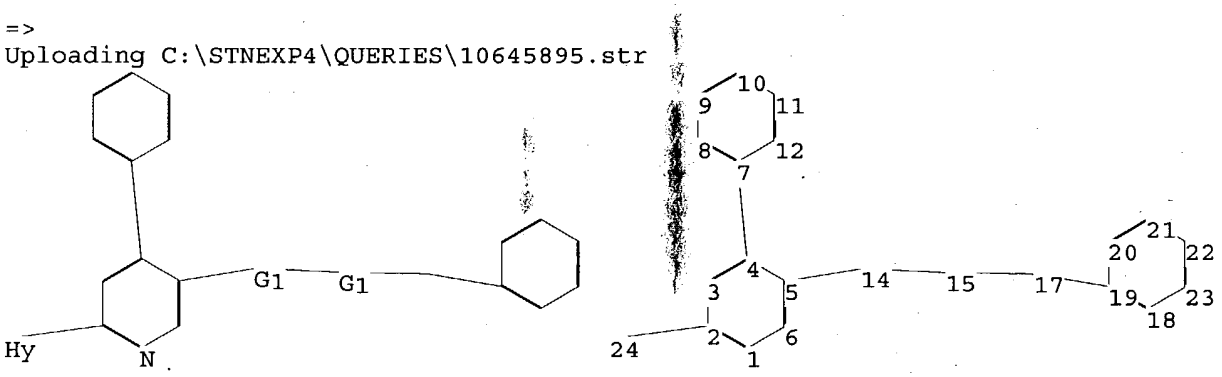

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normalized bonds :
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G1:C,O,N

Match level :
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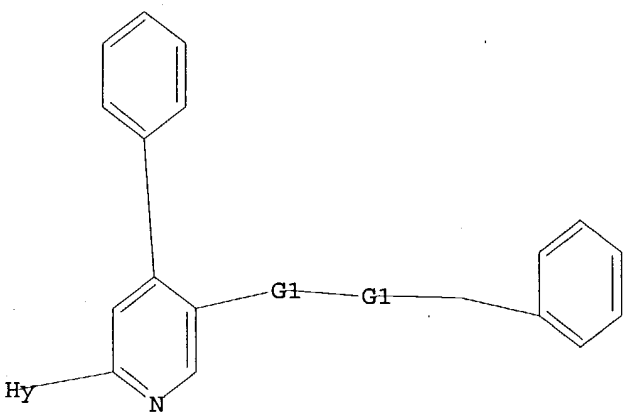

G1 C,O,N

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 1523 TO ITERATE

65.7% PROCESSED 1000 ITERATIONS 8 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
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FILE COVERS 1907 - 4 Feb 2004  VOL 140 ISS 6
FILE LAST UPDATED: 3 Feb 2004  (20040203/ED)

  This file contains CAS Registry Numbers for easy and accurate
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L5             1 L4 AND PD<AUGUST 2000

=> dis l5 bib abs hitstr

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1998:105938  CAPLUS
DN   128:167354
TI   Preparation of substituted pyridines and biphenyls as anti-
     hypercholesteremic, anti-hyperlipoproteinemic and anti-hyperglycemic
```

agents
IN Schmidt, Gunter; Angerbauer, Rolf; Brandes, Arndt; Muller-Gliemann, Matthias; Bischoff, Hilmar; Schmidt, Delf; Wohlfeil, Stefan; Schoen, William R.; Ladouceur, Gaetan H.; Cook, James H., II; Lease, Timothy G.; Wolanin, Donald J.; Kramss, Richard H.; Hertzog, Donald L.; Osterhout, Martin H.
PA Bayer Corporation, USA; Bayer Aktiengesellschaft
SO PCT Int. Appl., 431 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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OS MARPAT 128:167354
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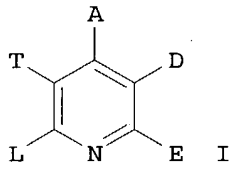

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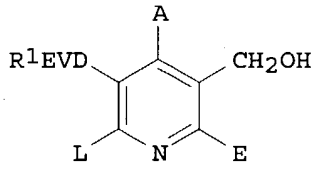

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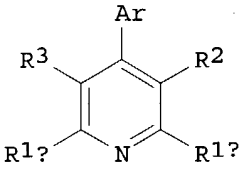

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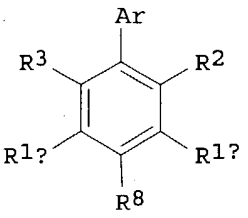


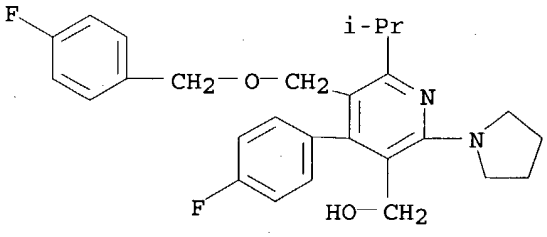
IV

AB The title compds. [I (A = (un)substituted C6-10 aryl; D = up to 8 carbon atoms alkyl which is substituted by hydroxy; E, L = (un)substituted up to 8 carbon atoms alkyl; L = (un)substituted C6-10 aryl; T = R7X, R8C(R9)(R10); R7, R8 = cycloalkyl, aryl, etc.; R9, R10 = H, halo, N3, etc.), II (R1 = cycloalkyl, aryl, etc.; E, D = alkyl (up to 8 carbon atoms); E = a bond; V = O, S, NH, etc.), III (R1a, R1b = CF3, C1-10 alkyl, C1-10 alkenyl, etc.; R2 = C1-10 alkyl, C1-10 alkenyl, etc.; R3 = OH, CF3, C1-6 alkanoyl, etc.; Ar = (un)substituted heteroaryl, aryl), IV], useful for the inhibition of cholesterol ester transfer proteins (CETP) (I), for the treatment of hyperlipoproteinemia (II), and for inhibition of the glucagon receptor, leading to treatment of glucagon-mediated conditions such as diabetes (III-IV), were prepared Thus, reduction of Et 2,6-diisopropyl-4-(4-fluorophenyl)-3-[(4-fluorophenyl)-chloromethyl]pyridine-5-carboxylate (preparation described) with LiAlH4 in THF afforded 69% I [A = 4-FC6H4; D = CH2OH; E = L = iPr; T = 4-FC6H4CH2]. For example, compound I [A = 4-FC6H4; D = CH2OH; E = L = iPr; T = 4-FC6H4CH(NH2)] showed IC50 of 0.6 μM against CETP.

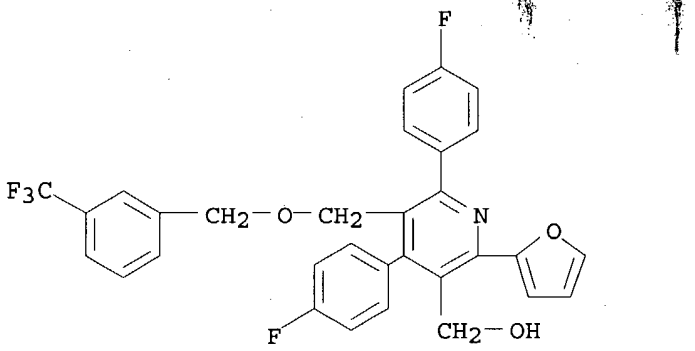
IT **202852-05-9P 202852-97-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted pyridines and biphenyls as anti-hypercholesteremic, anti-hyperlipoproteinemic and anti-hyperglycemic agents)

RN 202852-05-9 CAPLUS

CN 3-Pyridinemethanol, 4-(4-fluorophenyl)-5-[[(4-fluorophenyl)methoxy]methyl]-6-(1-methylethyl)-2-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)



RN 202852-97-9 CAPLUS
CN 3-Pyridinemethanol, 4,6-bis(4-fluorophenyl)-2-(2-furanyl)-5-[[[3-(trifluoromethyl)phenyl]methoxy]methyl]- (9CI) (CA INDEX NAME)



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L2 8 S L1 SAM
L3 139 S L1 FULL

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L6 14 L4 NOT L5

=> dis l6 1-14 bib abs

L6 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:737759 CAPLUS
DN 139:261291
TI Preparation of condensed heterocyclic compounds such as 5-oxo-7,8,9,9a-tetrahydro-5H-pyrido[2,3-a]pyrrolizine derivatives as calcitonin agonists
IN Bhandari, Ashok; Boros, Eric Eugene; Cowan, David John; Handlon, Anthony Louis; Hyman, Clifton Earl; Oplinger, Jeffrey Alan; Rabinowitz, Michael Howard; Turnbull, Philip Stewart
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DT Patent
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PI WO 2003076440	A1	20030918	WO 2003-US5605	20030224

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OS MARPAT 139:261291

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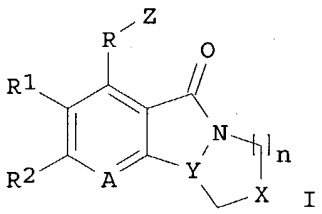


I

AB The title compds. [I; R = each (un)substituted aryl, heteroaryl, alkyl, or cycloalkyl, further wherein said aryl, heteroaryl, alkyl, or cycloalkyl; Z = H, alkyl, halogen, CO2R5, CON(R5)2, CONHN(R5)2, NHCON(R5)2, SO2N(R5)2, CH2NHCOR5, NO2, N(R5)2, NHCOR5, N(R5)SO2N(R5)2, OR5, CH2N(R5)2, CH2CON(R5)2, CH2CO2R5, (un)substituted heteroaryl; R5 = independently H, alkyl, trifluoromethyl, each (un)substituted aryl, heteroaryl, aralkyl, heteroaralkyl, cycloalkyl, heterocyclyl, fused cycloalkylaryl, or fused heterocyclylaryl; R1 = H, alkyl, CO2R5, COR5, CON(R5)2, cyano, NO2, N(R5)2, SO2R5, SO2N(R5)2, NHCOR5, NHCON(R5)2; R2 = alkyl, CF3, alkoxy, aryl, heteroaryl, aralkyl, heteroaralkyl, alkoxyaryl, further wherein said alkyl, aryl, heteroaryl, aralkyl, and heteroaralkyl may be substituted with one or more of halogen, CF3, or alkoxy; or R1 and R2 combine to form a 5- or 6-membered ring, optionally containing one or more heteroatom, optionally containing one or more degrees of unsatn., and optionally substituted one or more times with oxo, hydroxy, halogen, alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl, further wherein said alkyl, aryl, heteroaryl, aralkyl, and heteroaralkyl may be substituted with one or more of halogen, CF3, or alkoxy; A = C, N; Y = C, N; X = S, O, N(R5), C(R5)2, SO2; n = 1, 2, 3, or 4], salts, solvates, and pharmaceutically functional derivs. thereof are prepared These compds. are useful in the treatment and prevention of diseases or conditions which are related to irregular calcification or those mediated by calcitonin. They are used in therapies for osteopenia and osteoporosis in men and women; reduction in the risk of fractures, both vertebral and nonvertebral; Paget's disease; bone fracture or deficiency; primary or secondary hyperparathyroidism; periodontal disease or defect; metastatic bone disorder; osteolytic bone disease; post-plastic surgery; post-prosthetic joint surgery; postdental implantation; hypercalcemia; bone pain, general pain, and hyperalgesia; conditions associated with inhibiting gastric secretion; gastrointestinal disorders; osteoarthritis and rheumatoid arthritis; renal osteodystrophy; obesity by induction of satiety; and male infertility. Thus, 4-[3-(Ethoxycarbonyl)-2-[2-(4-fluorophenyl)ethyl]-5-oxo-8,9-dihydro-5H,7H-pyrazolo[1'2':1,2]pyrazolo[3,4-b]pyridin-4-yl]benzoic acid was condensed with furfurylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and HOBT-H2O in DMF at room temperature for 4 h to give 2-[2-(4-fluorophenyl)ethyl]-4-[4-[[(2-furylmethyl)amino]carbonyl]phenyl]-5-

oxo-8,9-dihydro-5H,7H-pyrazolo[1',2':1,2]pyrazolo[3,4-b]pyridine-3-carboxylate (II). In an CRE-luciferase reporter assay, II activated the human calcitonin-2 receptor (HCT2R) expressed in CHO-6CRE-luciferase cells with E50 of ≤10 nM.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:610660 CAPLUS
DN 139:160766
TI A method for correlating the preprotachykinin gene (NKNA) polymorphisms with the efficacy and compatibility of a pharmaceutically active compounds, such as NK-1 receptor antagonists
IN Foernzler, Dorothee; Hashimoto, Lara; Li, Jia; Luedin, Eric; Sleight, Andrew; Vankan, Pierre
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003064685	A2	20030807	WO 2003-EP630	20030123
WO 2003064685	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003158187	A1	20030821	US 2003-354693	20030130
PRAI EP 2002-1937	A	20020131		

AB The present invention relates to a method for correlating single nucleotide polymorphisms in the preprotachykinin (NKNA) gene with the efficacy and compatibility of a pharmaceutically active compound administered to a human being. The invention further relates to a method for determining the efficacy and compatibility of a pharmaceutically active compound administered to a human being which method comprises determining at least one single nucleotide polymorphism in the NKNA gene. Said methods are based on determining specific single nucleotide polymorphisms in the NKNA gene and determining the efficacy and compatibility of a pharmaceutically active compound in the human by reference to polymorphism in NKNA. The invention further relates to isolated nucleic acids comprising within their sequence the polymorphisms as defined herein, to nucleic acid primers and oligonucleotide probes capable of hybridizing to such nucleic acids and to a diagnostic kit comprising one or more of such primers and probes for detecting a polymorphism in the NKNA gene, to a pharmaceutical pack comprising neurokinin-1 (NK-1) receptor antagonists and instructions for administration of the drug to human beings tested for the polymorphisms as well as to a computer readable medium with the stored sequence information for the polymorphisms in the NKNA gene.

L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:117823 CAPLUS

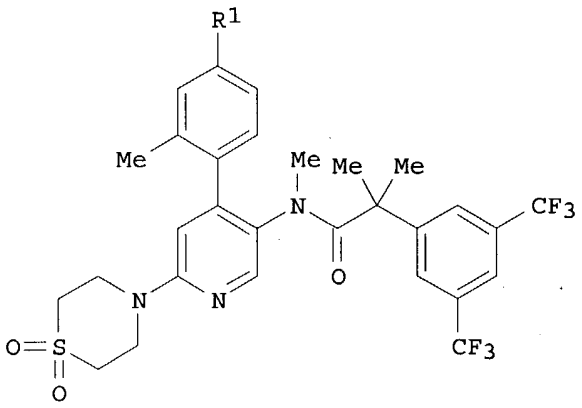
DN 138:170243
TI Preparation of 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-(2-methyl or 4-fluoro-2-methyl substituted)phenyl-pyridin-3-yl]-N-methyl-isobutyramide as selective NK1 antagonists
IN Ballard, Theresa Maria; Hoffmann, Torsten; Poli, Sonia Maria; Schnider, Patrick; Sleight, Andrew
PA F. Hoffmann-La Roche AG, Switz.
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003011860	A2	20030213	WO 2002-EP8311	20020726
WO 2003011860	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003064983	A1	20030403	US 2002-196795	20020717
PRAI EP 2001-118412	A	20010731		

OS MARPAT 138:170243
GI



I

AB The title compds. I [R1 = H, F] which may be used for the treatment of migraine, rheumatoid arthritis, asthma, bronchial hyperreactivity, inflammatory bowel disease or for the treatment of disorders including Parkinson's disease, anxiety, depression, pain, headache, Alzheimer's disease, multiple sclerosis,edema, allergic rhinitis, Crohn's disease, ocular injury, ocular inflammatory diseases, psychosis, motion sickness, induced vomiting, emesis, urinary incontinence, psychoimmunol. or

psychosomatic disorders, cancer, withdrawal symptoms of addictive drugs from opiates or nicotine, traumatic brain injury or benign prostatic hyperplasia, were prepared and formulated. E.g., a 8-step synthesis of I [R1 = H] (starting with 2-chloro-5-nitropyridine and thiomorpholine) which showed pKi of 8.9 for the human NK1 receptor, was given.

L6 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:57902 CAPLUS
DN 138:117662
TI Use of NK-1 receptor antagonists for the treatment of brain, spinal or nerve injury
IN Hoffmann, Torsten; Nimmo, Alan John; Sleight, Andrew; Vankan, Pierre; Vink, Robert
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

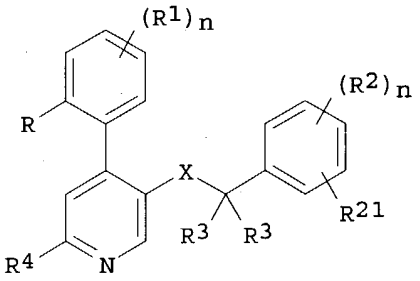
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006016	A2	20030123	WO 2002-EP7323	20020703
	WO 2003006016	A3	20030731		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003083345	A1	20030501	US 2002-187587	20020702
PRAI	EP 2001-116812	A	20010710		

OS MARPAT 138:117662
AB The invention discloses the use of an NK-1 receptor antagonist (Markush included), e.g. N-(3,5-bis-trifluoromethylbenzyl)-N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide, optionally in combination with a magnesium salt, for the treatment and/or prevention of brain, spinal or nerve injury. The invention also relates to pharmaceutical compns. comprising one or more such NK-1 receptor antagonists, optionally in combination with a magnesium salt, and a pharmaceutically acceptable excipient, for the treatment and/or prevention of brain, spinal or nerve injury.

L6 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:832668 CAPLUS
DN 137:337901
TI Preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia
IN Buser, Susanne; Ford, Anthony P. D. W.; Hoffmann, Torsten; Lenz, Barbara; Sleight, Andrew John; Vankan, Pierre
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	WO 2002085458	A2	20021031	WO 2002-EP1085	20020202
	WO 2002085458	A3	20031030		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1385577	A2	20040204	EP 2002-719751	20020202
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003004157	A1	20030102	US 2002-71570	20020208
PRAI	EP 2001-109853	A	20010423		
	WO 2002-EP1085	W	20020202		
OS	MARPAT 137:337901				
GI					



I

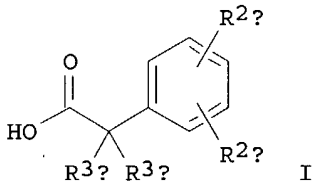
AB Use of an NK-1 receptor antagonist for the treatment or prevention of benign prostatic hyperplasia (BPH) is claimed. The preferred NK-1 receptor antagonists are compds. of the general formula [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H , halo , CF3, alkyl, alkoxy, cyano; R2R21 = CH:CHCH:CH, optionally substituted by 1-2 alkyl, halo, alkoxy; R3 = H, alkyl; R3R3C = cycloalkyl; R4 = H, N(R5)2, NR5(CH2)nOH, cyclic tertiary amine, etc.; X = CONR5, (CH2)pO, NR5(CH2)p, etc.; R5 = H, cycloalkyl, Ph, PhCH2, alkyl; n = 0-4; p = 1-3]. Preferred compds. are 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)isobutyramide, 3-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methylisobutyramide, and 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-thiomorpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide (preparation given) oxone were stirred 2 days at room temperature to give 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1λ6-thiomorpholin-4-yl)-4-o-tolylpyridin-3-yl]-N-methylisobutyramide. 2-(3,5-Bistrifluoromethylphenyl)-N-methyl-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide at 60 mg/kg/day orally in dogs reduced prostate weight by 58% after 39 wk.

L6 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:777873 CAPLUS
DN 137:294768
TI Acid-catalyzed carbonylation process for the manufacture of phenylacetic acid derivatives
IN Hoffmann-Emery, Fabienne; Scalone, Michelangelo; Spurr, Paul
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002079134	A1	20021010	WO 2002-EP1271	20020207
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002156313	A1	20021024	US 2002-41123	20020108
	US 6531597	B2	20030311		
	EP 1368295	A1	20031210	EP 2002-735104	20020207
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	EP 2001-103284	A	20010213		
	EP 2001-127405	A	20011123		
	WO 2002-EP1271	W	20020207		

OS CASREACT 137:294768; MARPAT 137:294768
GI



I

AB A process for the preparation of phenylacetic acid derivs. I [R2a-2b = H, halo, alkoxy, CN, COOH, alkoxycarbonyl, alkyl; R3a-3b = H, alkyl, cycloalkyl or taken together (CH2)n; n = 2,3,5] was disclosed. The process involves reacting an aryl Grignard derivative with a compound a carbonyl derivative followed by carbonylating the resulting carbinol in the presence of a strong acid. For instance, acetone was added to the Grignard reagent derived from 3,5-bis(trifluoromethyl)bromobenzene (Et2O, 16-22°) and the resulting carbinol (14.13 g) in CH2Cl2 pumped into a solution of CH2Cl2/CF3SO3H/H2O/CO at 30 bar at 20°. Aqueous work-up produced 14.98 g of 2-(3,5-bis(trifluoromethyl)phenyl)-2-methylpropionic acid with 99.0% purity. The carboxylic acid was converted to the acid chloride and then to a therapeutically active morpholine derivative in another example. The current process produces α,α-dialkylated carboxylic acid derivs. with fewer byproducts than prior art methods.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:465794 CAPLUS
DN 137:37665
TI Self-emulsifying lipid matrix (SELM) for oral pharmaceuticals
IN Kuentz, Martin; Roethlisberger, Dieter
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047663	A1	20020620	WO 2001-EP14437	20011208
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002016085	A5	20020624	AU 2002-16085	20011208
	EP 1349541	A1	20031008	EP 2001-270324	20011208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001016121	A	20031014	BR 2001-16121	20011208
	US 2002114837	A1	20020822	US 2001-15925	20011210
PRAI	EP 2000-127414	A	20001214		
	WO 2001-EP14437	W	20011208		

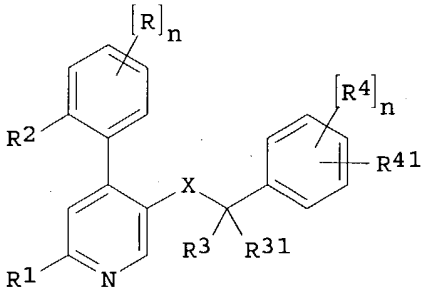
AB A pharmaceutical composition for oral administration of an active compound showing a bioavailability of 20% or less comprises (by weight) 0.01-15% of an active compound molecularly dissolved in the composition, 30-80% of an edible lipid matrix, and 1-20% of an edible emulsifier, the ratio between the dose weight of the active compound and its solubility in the composition being equal to or greater then 0.6 mL. The high percentage of fat (30-80%) enables to considerably increase the amount of the drug molecularly dispersed in the dosage form, thus allowing to significantly reduce the number of unit doses which must be taken daily by patients. For example, 8 g Cremophor RH 40 were dispersed in 70.08 g of cocoa butter, previously warmed to 70-80°. The temperature of the resulting mixture was then reduced to about 50-60° and 1.4 g of 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl) isobutyramide (I) were dissolved together with 0.02 g vanillin. The temperature of the resulting mixture was further reduced to 40° and 0.5 g aspartame were added. Finally, 20 g of milk powder were added at about 35° (upper limit of the melting interval of cocoa butter). The resulting homogeneous mixture was then dosed in molds whereby SELM tablets of 5 g each (corresponding to a volume of about 5 mL) were obtained showing a ratio between the dose weight of the active compound and its solubility in the composition of at least 4.67 mL. The use of SELM composition enabled an increase of the bioavailability of I up to 22% in beagle dogs.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:157739 CAPLUS
DN 136:216651
TI Preparation of 4-phenylpyridines as neurokinin-1 receptor antagonists
IN Godel, Thierry; Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002016324	A1	20020228	WO 2001-EP8686	20010727
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002012118	A5	20020304	AU 2002-12118	20010727
	EP 1309559	A1	20030514	EP 2001-980219	20010727
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001013173	A	20030624	BR 2001-13173	20010727
	US 2002040040	A1	20020404	US 2001-922066	20010803
	NO 2003000632	A	20030207	NO 2003-632	20030207
PRAI	EP 2000-117003	A	20000808		
	WO 2001-EP8686	W	20010727		

OS MARPAT 136:216651
GI



I

AB The title compds. [I; R = H, halo; R1 = (C.tplbond.C)mR11, (CR'=CR'')mR11 (wherein R11 = halo, CN, aryl, etc.; R', R'' = H, OH, alkyl, etc.); R2 = H, alkyl, alkoxy, halo, CF3; R3, R31 = H, alkyl or form together with the C atom to which they are attached a cycloalkyl group; R4, R41 = H, halo, CF3, alkyl, alkoxy; R and R2 or R4 and R41 may be together CH=CHCH=CH, optionally substituted by one or two substituents selected from alkyl, halo or alkoxy; X = CONR8, (CH2)pO, (CH2)pNR8, NR8CO, NR8(CH2)p (wherein

R8 = H, alkyl); n = 1-2; m = 0-4; p = 1-2] which are antagonists of the Neurokinin 1 (NK-1, substance P) receptor, and therefore useful in the treatment of diseases, related to this receptor, were prepared and formulated. E.g., a multi-step synthesis of I [R = H; R1 = N(OH)CH2CH2OH; R2 = Me; R3, R31 = Me; R4 = 3-CF3; R41 = 5-CF3; X = NMeCO] which showed pKi of 9.29 in human NK1 receptor assay, was given.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:90050 CAPLUS
DN 136:134681
TI Preparation of 4-phenylpyridine derivatives as neurokinin-1 receptor antagonists
IN Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002008232	A1	20020131	WO 2001-EP8432	20010720
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002038030	A1	20020328	US 2001-901311	20010709
	US 6576762	B2	20030610		
	BR 2001012695	A	20030422	BR 2001-12695	20010720
	EP 1305319	A1	20030502	EP 2001-960529	20010720
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003130508	A1	20030710	US 2002-282357	20021029
	US 6624176	B2	20030923		
	NO 2003000353	A	20030123	NO 2003-353	20030123
PRAI	EP 2000-115846	A	20000724		
	US 2001-901311	A1	20010709		
	WO 2001-EP8432	W	20010720		

OS MARPAT 136:134681
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

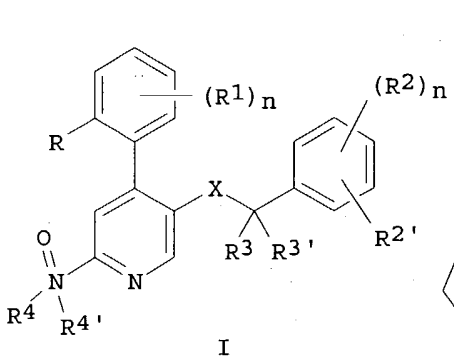
AB The title compds. [I or II; R1 = III, 2,3-dihydro-[1,4]oxazin-4-yl, imidazol-1-yl, [1,2,4]triazol-1-yl, NH(CH2)2OH, NR3COCH3, NR3COcyclopropyl; R2 = Me, Cl; R3 = H, Me; R = H, (CH2)2OH; n = 1-2] which have a good affinity of the NK-1 receptor and therefore they may be used in the treatment or prevention of diseases, related to this receptor, were prepared and formulated. E.g., a multi-step synthesis of I [R1 = [1,2,4]triazol-1-yl; R2 = Me] which showed pKi of 8.4 against binding at

human NK1 receptors in CHO cells, was given.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:72051 CAPLUS
DN 136:118387
TI Preparation of N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivatives
IN Hoffmann, Torsten; Poli, Sonia Maria; Schnider, Patrick; Sleight, Andrew
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002006236	A1	20020124	WO 2001-EP7850	20010709
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1303490	A1	20030423	EP 2001-949475	20010709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001012475	A	20030729	BR 2001-12475	20010709
	US 2002045642	A1	20020418	US 2001-904059	20010712
	US 6593472	B2	20030715		
	HR 2003000003	A1	20030228	HR 2003-3	20030102
	US 2003149039	A1	20030807	US 2003-337543	20030107
	NO 2003000154	A	20030113	NO 2003-154	20030113
	US 2004014793	A1	20040122	US 2003-616276	20030709
PRAI	EP 2000-115287	A	20000714		
	WO 2001-EP7850	W	20010709		
	US 2001-904059	A3	20010712		
	US 2003-337543	A3	20030107		

OS MARPAT 136:118387
GI



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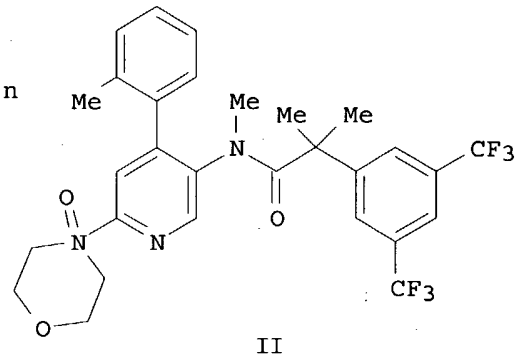


II

AB The preparation is described for N-oxides (I) wherein R is hydrogen, lower alkyl, lower alkoxy, or trifluoromethyl; R1 is hydrogen or halogen; or R and R1 may be together with the ring carbon atoms to which they are attached -CH=CH-CH=CH-; R2 and R2' are independently from each other hydrogen, halogen, trifluoromethyl, lower alkoxy or cyano; or R2 and R2' may be together -CH=CH-CH=CH-, optionally substituted by one or two substituents selected from lower alkyl or lower alkoxy; R3, R3' are independently from each other hydrogen, lower alkyl or cycloalkyl; R4, R4' are independently from each other -(CH2)mOR6 or lower alkyl; or R4 and R4' form together with the N-atom to which they are attached a cyclic tertiary amine with substituent R5 chosen from hydrogen, hydroxy, lower alkyl, -lower alkoxy, -(CH2)mOH, -COOR3, -CON(R3)2,-N(R3)CO-lower alkyl or -C(O)R3; R6 is hydrogen, lower alkyl or phenyl; X is -C(O)N(R6)-, -N(R6)C(O)-, -(CH2)mO- or -O(CH2)m-; n is 0, 1, 2, 3 or 4 and; m is 1, 2, or 3; and to their pharmaceutically acceptable acid addition salts. These compds. may be uses as prodrugs for the treatment or prevention of illnesses, related to the NK1 receptor. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-[6-(4-oxymorpholin-4-yl)-4-o-tolylpyridin-3-yl]isobutyramide (II) and related compds. were prepared in multistep procedures.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

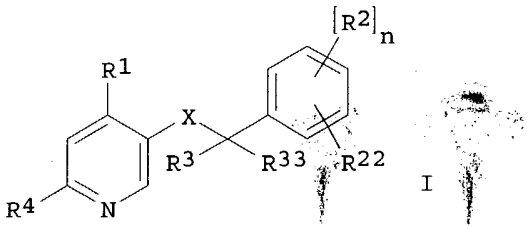
L6 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:396485 CAPLUS
DN 135:5533
TI Process for preparation of pyridine derivatives
IN Hilpert, Hans; Hoffmann-Emery, Fabienne; Rimmler, Goesta; Rogers-Evans, Mark; Stahr, Helmut Werner; Waldmeier, Pius
PA F. Hoffmann-La Roche A.-G., Switz.
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1103546	A1	20010530	EP 2000-125665	20001123
	EP 1103546	B1	20031022		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6303790	B1	20011016	US 2000-716538	20001120
	AT 252559	E	20031115	AT 2000-125665	20001123

	JP 2001151755	A2	20010605	JP 2000-360682	20001128
	JP 3403164	B2	20030506		
	CN 1297887	A	20010606	CN 2000-128383	20001128
PRAI	EP 1999-123686	A	19991129		

OS CASREACT 135:5533; MARPAT 135:5533

GI



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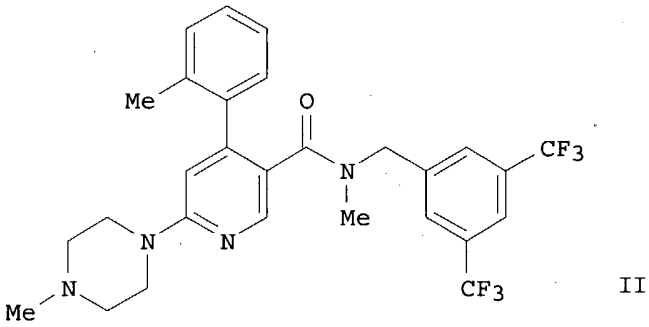


II

AB The title compds. [I; R1 = alkyl, (un)substituted aryl; R2, R22 = H, halo, CF3, etc.; R2 and R22 may be together = (un)substituted CH:CHCH:CH; R3, R33 = H, alkyl, or forming a cycloalkyl together with the carbon atom, to which they are attached; R4 = H, alkyl, (un)substituted NH2, etc.; X = CONR5, NR5CO; R5 = H, alkyl, CH2Ph; n = 0-4], useful as antagonists of neurokinin 1 receptor (no data), were prepared Thus, treating 6-chloronicotinic acid with SOCl2 and MeNH2.HCl followed by reaction of 6-chloro-N-methylnicotinamide with o-tolylmagnesium chloride and 1-methylpiperazine, treatment of 6-(4-methylpiperazin-1-yl)-4-o-tolyl-4,5-dihydropyridine-3-carboxylic acid methylamide with MnO2, and reacting N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide with 3,5-bis(trifluoromethyl)benzyl bromide afforded the nicotinamide II.

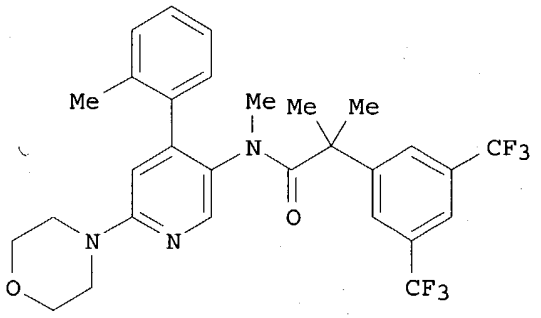
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:396484 CAPLUS
DN 135:5620
TI Preparation of 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-[6-(morpholin-4-yl)-4-(o-tolyl)-pyridin-3-yl]-isobutyramide for the treatment of diseases related to the NK-1 receptor
IN Ballard, Theresa Maria; Higgins, Guy Andrew; Hoffmann, Torsten; Poli, Sonia Maria; Sleight, Andrew
PA F. Hoffmann-La Roche A.-G., Switz.

SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1103545	A1	20010530	EP 2000-125450	20001121
EP 1103545	B1	20031105		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 253561	E	20031115	AT 2000-125450	20001121
GB 2356863	A1	20010606	GB 2000-28566	20001123
NZ 508386	A	20030228	NZ 2000-508386	20001123
DE 10058310	A1	20010531	DE 2000-10058310	20001124
FR 2801590	A1	20010601	FR 2000-15193	20001124
JP 2001151754	A2	20010605	JP 2000-356833	20001124
JP 3480835	B2	20031222		
HR 2000000809	A1	20011231	HR 2000-809	20001124
SG 97171	A1	20030718	SG 2000-6945	20001124
ZA 2000006964	A	20010605	ZA 2000-6964	20001127
NO 2000006012	A	20010530	NO 2000-6012	20001128
BR 2000005616	A	20010717	BR 2000-5616	20001128
BG 104992	A	20011130	BG 2000-104992	20001128
ES 2171134	A1	20020816	ES 2000-2839	20001128
CN 1297888	A	20010606	CN 2000-134260	20001129

PRAI EP 1999-123685 A 19991129
GI



I

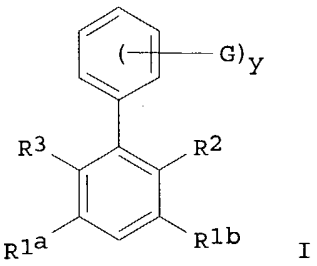
AB The title compound I which is a potent and selective antagonist at recombinant human neurokinin1 (NK1) receptors expressed in CHO cells, was prepared (details of multi-step synthesis were given) and formulated. The compound I showed an affinity (pKi) of 9.0 for the human NK1 receptor over 2 orders of magnitude of selectivity for the NK1 receptor compared to NK2 and NK3 receptors and compared to over 50 other binding sites that have been evaluated.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:278024 CAPLUS
DN 134:311111
TI Preparation of substituted biphenyls as glucagon receptor antagonists
IN Schoen, William R.; Ladouceur, Gaetan H.; Cook, James H., II; Lease, Timothy G.; Wolanin, Donald J.; Kramss, Richard H.; Hertzog, Donald L.;

Osterhout, Martin H.
PA Bayer Corporation, USA; Bayer A.-G.
SO U.S., 156 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6218431	B1	20010417	US 1997-904119	19970731
PRAI US 1997-904119		19970731		

OS MARPAT 134:311111
GI



I

AB Substituted biphenyls I [R1a, R1b = alkyl; R2 = alkyl with substituents from 1 to 3 of SR7; R7 = Ph, or substituted Ph wherein the substituents are independently 1-5 of halogen, trifluoromethyl, alkyl, alkoxy, nitro, cyano, hydroxyl; R3 = alkyl with substituents of 1-2 hydroxyl groups; G represents a substituent selected from the group consisting of halogen, alkyl, OR4 with R4 = H, alkyl; y = 0-3], glucagon receptor antagonists. E.g., reduction of 2-cyclopentyl-6-ethyl-4-(4-fluorophenyl)-3-(3-trifluoromethylbenzyloxymethyl)pyridine-5-carboxylic acid Et ester with LiAlH4 gave 76.5% 2-cyclopentyl-6-ethyl-4-(4-fluorophenyl)-5-hydroxymethyl-3-(3-trifluoromethylbenzyloxymethyl)pyridine.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:607348 CAPLUS
DN 133:207811
TI Preparation of N-benzyl-4-tolylnicotinamides and related compounds as neurokinin-1 receptor antagonists.
IN Boes, Michael; Branca, Quirico; Galley, Guido; Godel, Thierry; Hoffmann, Torsten; Hunkeler, Walter; Schnider, Patrick; Stadler, Heinz
PA F. Hoffmann-La Roche Ag, Switz.
SO Ger. Offen., 38 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10008042	A1	20000831	DE 2000-10008042	20000222
EP 1035115	A1	20000913	EP 2000-102260	20000215

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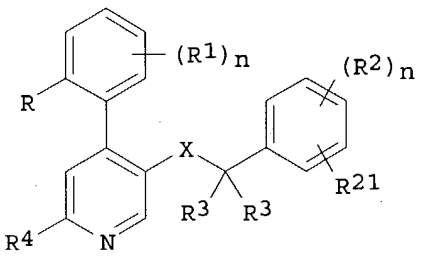
	GB 2347422	A1	20000906	GB 2000-3908	20000218
	NZ 502948	A	20010928	NZ 2000-502948	20000218
	FR 2790473	A1	20000908	FR 2000-2170	20000222
	US 6297375	B1	20011002	US 2000-507456	20000222
	CA 2299139	AA	20000824	CA 2000-2299139	20000223
	ZA 2000000894	A	20000824	ZA 2000-894	20000223
	NO 2000000885	A	20000825	NO 2000-885	20000223
	BR 2000000908	A	20000912	BR 2000-908	20000223
	CN 1270959	A	20001025	CN 2000-102401	20000223
	HR 2000000097	A1	20011031	HR 2000-97	20000223
	ES 2171109	A1	20020816	ES 2000-418	20000223
	SG 91856	A1	20021015	SG 2000-1033	20000223
	JP 2000247957	A2	20000912	JP 2000-47003	20000224
	JP 3399900	B2	20030421		
	BG 104187	A	20001130	BG 2000-104187	20000224
	AU 767048	B2	20031030	AU 2000-19468	20000224
	AU 2000019468	A5	20000831		
	US 2002091265	A1	20020711	US 2001-901982	20010710
	US 6479483	B2	20021112		
PRAI	EP 1999-103504	A	19990224		
	EP 1999-123689	A	19991129		
	US 2000-507456	A3	20000222		

OS MARPAT 133:207811

GI



I

AB Title compds. [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H, halo, CF3, alkoxy, cyano; R2R21 = (substituted) CH:CHCH:CH; R3 = H, alkyl, cycloalkyl; R4 = H, N(R5)2, N(R5)(CH2)nOH, N(R5)S(O)2A, N(R5)S(O)2Ph, N:CHN(R5)2, N(R5)C(O)R5, specified cyclic tertiary amine; R5 = H, cycloalkyl, benzyl, alkyl; X = C(O)N(R5), (CH2)mO, (CH2)mN(R5), N(R5)C(O), N(R5)(CH2)m; n = 0-4; m = 1, 2], were prepared Thus, 4-o-tolylnicotinic acid (preparation given) was stirred with SOCl2 and cat. DMF in CH2Cl2 to give a residue which was refluxed with N-[3,5-bis(trifluoromethyl)benzyl]-N-methylamine and Et3N in PhMe to give 67% N-(3,5-bistrifluoromethylbenzyl)-N-methyl-4-o-tolylnicotinamide. Tested I antagonized NK-1 receptors with pKi = 8.20-9.54.

=> file caold

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	43.02	198.65

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE -10.40 -10.40

FILE 'CAOLD' ENTERED AT 13:35:57 ON 04 FEB 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s l3
L7 0 L3

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	199.07

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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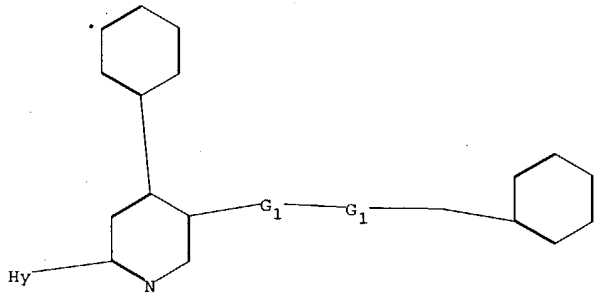

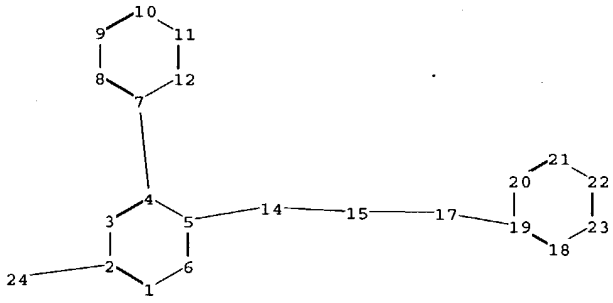

chain nodes :
14 15 17 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 18 19 20 21 22 23
chain bonds :
2-24 4-7 5-14 14-15 15-17 17-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 18-19 18-23 19-20
20-21 21-22 22-23
exact/norm bonds :
2-24 5-14 14-15 15-17
exact bonds :
4-7 17-19
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 18-19 18-23 19-20
20-21 21-22 22-23
isolated ring systems :
containing 1 :

G1:C,O,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 14:CLASS 15:CLASS 17:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom
24:Atom
Generic attributes :
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Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic